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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/695,644

10/29/2003

David S. Garvey

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05/15/2006

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EXAMINER

AULAKH, CHARANJIT

ART UNIT

PAPER NUMBER

1625

DATE MAILED: 05/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/695,644	<b>Applicant(s)</b> GARVEY, DAVID S.	
	<b>Examiner</b> Charanjit S. Aulakh	<b>Art Unit</b> 1625	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 April 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3-6, 11, 16-24, 29, 35-39, 44, 48, 50, 55, 59, 61, 66-70, 72-76, 80-82 and 91 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>1 page</u> .  | 6) <input type="checkbox"/> Other: _____                                    |

Continuation of Disposition of Claims: Claims pending in the application are 3-6,11,16-24,29,35-39,44,48,50,55,59,61,66-70,72-76,80-82 and 91.

### **DETAILED ACTION**

1. According to paper filed on April 24, 2006, the applicants have filed RCE; canceled claims 1, 2, 7-10, 12-15, 25-28, 30-34, 40-43, 45-47, 49, 51-54, 56-58, 60, 62-65, 71, 77-79, 83-90 and 92 and furthermore, have amended claims 3, 6, 16, 19-24, 35, 36, 39, 48, 50, 59, 61, 76, 81 and 91.
2. Claims 3-6, 11, 16-24, 29, 35-39, 44, 48, 50, 55, 59, 61, 66-70, 72-76, 80-82 and 91 are now pending in the application.

### ***Response to Arguments***

3. Applicant's arguments filed on April 24, 2006 have been fully considered but they are not persuasive regarding enablement rejection, some indefiniteness rejections and obviousness rejection. In regard to enablement rejection, the examiner does not agree with the applicants arguments that the specification is enabling for treating hypertension using instant compounds of formula I in combination with hundreds of thousands of other drugs. The antihypertensive effect of nebivolol is well known in the prior art based on its beta-adrenergic receptor antagonist activity. There is no teaching either in the specification or prior art regarding well known utility of treating hypertension of combination of bet-adrenergic antagonists and hundreds of thousands of drugs encompassed by instant claims. Also, in regard to instant compounds of formulae IV and V, there is no teaching in the specification or prior art that these metabolites are known to have beta-adrenergic receptor antagonist activity or therapeutic utility of treating hypertension. There is no teaching in the prior art and furthermore, there are no working examples present in the instant specification showing efficacy of instant

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compounds of formulae IV and V alone or in combination with any other drug in animal models of hypertension. Similarly, there is no teaching in the prior art and furthermore, there are no working examples present showing efficacy of instant compounds of formula I in combination with any other drug in animal models of hypertension. In summary, the specification is enabling for treating hypertension using instant compounds of formula I only based on prior art studies. In regard to indefiniteness rejections of instant claims 48, 59, 76 and 91, the examiner does not agree with the applicants arguments that these classes of compounds are well known and therefore, need not to be defined. In regard to obviousness rejection, the examiner does not agree with the applicants arguments that it would not have been obvious to one skilled in the art to arrive at the instant claimed invention. Loscalzo teaches treating vascular diseases including hypertension by nitrosated beta-adrenergic antagonists including Nebivolol and Von Lommen teaches increased beta-adrenergic antagonist activity of Nebivolol as compared to other known beta-adrenergic antagonists for treating hypertension also. Therefore, one skilled in the art would have been motivated to select nitrosated Nebivolol as beta-adrenergic antagonist due to its greater efficacy and well known structure as taught by Von Lommen.

### ***Conclusion***

4. The enablement rejection of claims 5, 6, 11, 16-24, 29, 35-39, 44, 48, 50, 55, 59, 61, 66-70, 72-76, 80-82 and 91 under 35 U.S.C. 112, first paragraph is maintained for the reasons of record.

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5. The indefiniteness rejections of claims 48, 59, 76 and 91 under 35 U.S.C. 112, second paragraph are maintained for the reasons of record.

6. The obviousness rejection of claims 3-6, 11, 16-24, 29, 35-39, 44, 48, 50, 55, 59, 61, 66-70, 72-76, 80-82 and 91 under 35 U.S.C. 103(a) is maintained for the reasons of record.

NEW GROUNDS OF REJECTION

***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 17 and 18 recite the limitation "N-acetylcysteine, captopril etc for thiol" in claim 16. There is insufficient antecedent basis for this limitation in the claim. Thiol represents SH group only.

In claims 19-21, the terms ---polypeptide, amino acid, sugar, oligonucleotide, heterocyclic group etc.--- are indefinite since specific structures are not defined and furthermore, it is not clear where NO or NO<sub>2</sub> group is attached?

Claim 22 recites the limitation "isosorbide dinitrate for O<sub>2</sub>N-O-sugar" in claim 21. There is insufficient antecedent basis for this limitation in the claim since the sugar can have only one NO<sub>2</sub> group.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on (571)272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Charanjit S. Aulakh  
Primary Examiner  
Art Unit 1625